REMARKS

Upon entry of the foregoing amendments, claims 1, 7-13, 15-23, 25-27 and 36-41 will be pending in the application. Composition claim 1 and process of use claims 26 and 27 are the only pending independent claims. The Examiner withdrew from consideration dependent delivery device claim 24, dependent process of preparation claim 25, and independent process of use claims 26 and 27 and their dependent process of use claims 36-41, since these were the claims that were not provisionally elected, with traverse. Non-elected delivery device claim 24 has been canceled without prejudice to its inclusion in a divisional application. Non-elected process of preparation claim 25, depending from claim 1, has not been canceled, non-elected independent process of use claims 26 and 27 have been amended, and non-elected process of use claims 36-41, dependent directly or indirectly from claims 26 or 27, have been retained in anticipation that they will be rejoined upon the indication of an allowable claim directed to the composition.

Explanation of and Support for the Amendments of the Claims

Claim 1 and independent process of use claims 26 and 27 have been amended, without prejudice, to recite that the composition is a low viscosity aqueous liquid at ambient temperature and that the chitosan, or a derivative thereof or a salt of chitosan or a salt of a derivative of chitosan (the chitosan ingredients being referred to hereinafter for the sake of convenience simply as "chitosan"), the polyol-phosphate or sugar-phosphate salt and triethyl citrate are in solution and the systemically-acting drug may be in solution or suspended in the aqueous solution. Support for the recitation of the viscosity of 150 cP or less at 25°C is at least at page 13, lines 1-5 and 16-18, of the Substitute Specification filed with the U.S. National Stage filing on August 21, 2006. The remaining amendments to claims 1, 26 and 27 are merely rewording of the prior language of such claims for purposes of clarity in view of the previously-mentioned amendment.

Since all of the foregoing amendments are supported by the application as filed and no new matter has been added, entry of the foregoing amendments is respectfully requested.

Obviousness Rejection Under 35 U.S.C. § 103(a)

The Examiner considered that the compositions as previously claimed would have been obvious in view of Chenite *et al.* U.S. Patent 6,344,488 ("Chenite") in view of Dunn *et al.* U.S. Patent 5,702,716 ("Dunn") and Illum U.S. Patent 5,629,011 ("Illum"). Applicants respectfully traverse this rejection.

The Examiner seems to consider that the most significant difference between the compositions of Chenite and those of the present invention is that the compositions of Chenite do not comprise triethyl citrate. The Examiner asserts that it would have been obvious in view of the teaching of Dunn to introduce triethyl citrate into the compositions of Chenite. Contrary to the Examiner's assertion, this would not have been an obvious thing for the skilled person to do at the time of the invention. However, some initial comments on the teaching of Chenite, as the primary reference, are in order.

The compositions of Chenite are aqueous. However, there is nothing in Chenite to suggest that these compositions may have a low viscosity at 25°C as required by the amended independent claims. At column 4, lines 40-41, of Chenite it is stated: "The polysaccharide gel solution may be kept in a stable ungelled liquid form at a temperature ranging from 0°C to about 20°C." [Emphasis added]. It is important to maintain the compositions of Chenite at these low temperatures because as the temperature increases the viscosity increases. The "gelating temperature" of Chenite's composition is defined "to mean any temperature ranging from about 20°C to about 80°C" at column 5, lines 50-51. Thus, since the 25°C temperature recited in the amended independent claims is within Chenite's "gelating temperature," the skilled person reading Chenite would not have expected the composition as described in Chenite to have the low viscosity as a liquid at 25°C required by the present invention, but instead would be a gel, rather than an aqueous solution as claimed in the present application.

The Examiner has turned to Dunn for motivation to introduce triethyl citrate into the compositions of Chenite. It is not realistic to combine the teachings of Chenite and Dunn. As discussed above, Chenite describes aqueous compositions and contrary to the Examiner's assertion, Dunn describes non-aqueous compositions.

As stated at column 2, lines 26-29, Dunn describes liquid compositions which are a combination of an organic solvent, a biocompatible, biodegradable thermoplastic polymer, a rate modifying agent and a bioactive material. In use, this composition forms a polymer system. As pointed out in several locations in Dunn, such as at column 2, lines 30-41, the polymer system is formed by applying the non-aqueous composition to an aqueous medium. After application, the liquid composition coagulates to form the polymer system. The polymer system is substantially insoluble in aqueous media. This is completely different from the compositions of the invention in which the chitosan, polyol-phosphate or sugar-phosphate salt and triethyl citrate and optionally the drug are dissolved in an aqueous solution.

Chitosan is listed at column 4, line 31, as a possible suitable thermoplastic polymer for use in the compositions of Dunn. However, chitosan is not used in any of the Examples of Dunn and claim 1 which includes a list of the thermoplastic polymers that may be used in the polymer system of Dunn does not list chitosan. In fact, the skilled person reading Dunn would have appreciated that chitosan is not and would not be a suitable thermoplastic polymer for use in the compositions of Dunn. It is stated at column 4, lines 63-67, of Dunn that preferred thermoplastic polymers have low solubility in water and high solubility in organic solvents. Chitosan and its salts and derivatives are insoluble in organic solvents. This was well known at the priority date and the skilled person reading Dunn would have realized that chitosan is not a suitable solvent for use in the compositions disclosed in that document. Therefore, for these reasons alone, the combination of Dunn with Chenite would not make sense and would not suggest the present invention.

The compositions of Dunn may also comprise a rate modifying agent. Suitable rate modifying agents include triethyl citrate. Although triethyl citrate is listed at column 8, line 47, as a preferred rate modifying agent, this is contrary to the teaching elsewhere in Dunn. At column 7, lines 48-57, it is stated that the rate modifying agent is preferably water insoluble. However, triethyl citrate is water soluble. Again, it is noted that triethyl citrate is not used in any of the examples of Dunn. Dunn most certainly does not provide any motivation to combine chitosan and triethyl citrate in an aqueous composition, particularly in view of the inconsistent teaching of Dunn about an insoluble rate modifying agent.

The compositions of Dunn function in an entirely different way compared to the

compositions of the present invention. As described above, in the compositions of the present invention the chitosan, the polyol-phosphate or sugar-phosphate salt and triethyl citrate are dissolved in an aqueous medium. The purpose of the inclusion of triethyl citrate in the compositions of the invention is to facilitate a rapid increase in viscosity and gelation at the physiological temperature. In contrast, the rate modifying agents used in Dunn are used to control the rate of drug release. The skilled person reading Dunn would have had no expectation that triethyl citrate would or even could increase the rate of gelation at physiological temperature of an aqueous composition comprising chitosan and a polyol-phosphate or sugar-phosphate salt while allowing the composition to have a low viscosity as defined in claim 1 at 25°C. This low viscosity at 25°C is important because a low viscosity is necessary to enable the composition to be delivered as a spray or as drops.

The manner in which the compositions of Dunn function in use is completely different from the way in which the compositions of the present invention function. As described at column 15, lines 7-11 of Dunn, contacting the organic composition of Dunn with an aqueous medium results in diffusion of the organic solvent into the aqueous medium and in coagulation of the thermoplastic polymer to form a solid microporous matrix. At no point in the practice of the invention of Dunn is an aqueous solution formed containing components as specified in claim 1 of the present application.

The teaching of Dunn is not relevant to the present invention and the skilled person starting from Chenite would not have considered the teaching of Dunn. Even if he had read Dunn (which is considered unlikely in view of the disparity of Chenite and Dunn), he would not have been motivated to make the modifications necessary to arrive at the present invention.

The Examiner suggested that Applicants should provide experimental data based on the teaching of Dunn. This is neither appropriate nor possible in view of the non-aqueous nature of Dunn's composition and the insolubility of chitosan in organic solvents.

Illum does not add anything to the teaching of Chenite or the teaching of Dunn, alone or in combination, that would have encouraged the skilled person to include triethyl citrate in the compositions of Chenite, or to modify the illogical prior combination of Chenite and Dunn. Illum does not even mention triethyl citrate anywhere in the patent. Illum describes compositions in the form of an aqueous solution or suspension for nasal delivery of a

therapeutic agent, contrary to Dunn's non-aqueous, insoluble, coagulated polymer system. However, there is nothing in Illum or in either of the other cited references that would have motivated a skilled person to combine the teaching of these documents. Chenite and Dunn are quite clearly directed to compositions that are intended to stay in the body for a considerable period of time, such as implants. If these compositions comprise a drug compound, that drug compound is released into the body over a period of days or longer. This is a completely different type of drug release and therapeutic application to that which is described in Illum. The skilled person seeking to produce a composition that could be prepared as a liquid aqueous solution at ambient temperatures, including the components claimed, and delivered with a systemically-acting therapeutic agent dissolved or suspended in the aqueous solution, such as by using a spray or drops, would not have considered the teaching of Chenite or Dunn, let alone the combination of both documents with Illum.

Reconsideration and withdrawal of the obviousness rejection are respectfully requested.

Moreover, reconsideration and withdrawal of the restriction requirement and the rejoinder of the provisionally non-elected claims, and an early Notice of Allowance with respect to all pending claims are respectfully requested.

Respectfully submitted,

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